PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 79. WO1	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/US2004/035927	International filing date *(day/month/year)* 29.10.2004	Priority date *(day/month/year)* 31.10.2003
International Patent Classification (IPC) or national classification and IPC C07D403/04, C07D495/04, C07D491/04, A61K31/41		
Applicant ARENA PHARMACEUTICALS, INC. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.02.2005	10.10.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Goss, I Telephone No. +49 89 2399-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/035927

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-85 as originally filed

   Claims, Numbers

   1-41 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

   * *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/035927

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 28-31

because:

☒ the said international application, or the said claims Nos. 28-31 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/035927

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-41
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-41
Industrial applicability (IA)	Yes:	Claims	1-27,32-41
	No:	Claims	28-31

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 28 to 31 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document/s/:

D1: WO 2004/032928 A (ARENA PHARM INC [US]; SEMPLE GRAEME [US]; AVERBUJ CLAUDIA [US]; SKINNE) 22 April 2004 (2004-04-22)

D2: EP-A-0 529 854 (ORTHO PHARMACEUTICAL CORPORATION) 3 March 1993 (1993-03-03)

D3: BAYS H ET AL: "PHARMACOTHERAPY FOR DYSLIPIDAEMIA - CURRENT THERAPIES AND FUTURE AGENTS" EXPERT OPINION ON PHARMACOTHERAPY, ASHLEY, LONDON,, GB, vol. 4, no. 11, 2003, pages 1901-1938, XP008027524 ISSN: 1465-6566

Novelty

The subject-matter claimed relates to 1H-tetrazole derivatives substituted by a bicyclic moiety carrying either a pyrazole or an isoxazole ring at position 5.
Document D2 describes tetrahydroindazole, tetrahydrocyclopentapyrazole, an hexahydrocycloheptapyrazole compounds never substituted by a tetrazole group.
D3 relates to the pharmacotherapy for dyslipidaemia and to the current and future lipid-altering drugs, none of which showing structural similarity to those presently claimed.
Novelty is therefore recognized.

Inventive step

The problem underlying the present application is seen in the provision of derivatives useful in the inhibition of the production of free fatty acids and more in general treatment of a metabolic-related disorder.

The compounds of the invention appear to modulate a RUP25 receptor. The compounds described in both D2 or D3 also show a similar pharmacological profile (even if the mechanism of action is actually not given in details as it is done in the present application) belong, however, to different structural families of compounds.
Thus, the skilled person faced with the problem of providing further useful compounds for the treatment of a health problem that is serious, widespread and increasing would not have taken an incentive from the prior art know so far to arrive at the claimed class of compounds. It appears, however, that assays have been described in the description without any quantitative results. As a consequence of this, it is difficult to ascertain if the problem underlying the invention has been indeed solved by the compounds provided and tested and if the whole scope claimed is justified by the tests results which are, at present, missed.
In this respect Applicant's attention is also drawn to the following remark:

The term "5,6 or 7-membered carbocyclic ring being optionally further substituted" used in claim 1, is considered to be non-limitative and embraces an infinite number of possibilities not yet explored by the Applicant (the examples only vary among cyclopenta, furo or thieno ring); it should therefore be limited to the specific meanings given in the description as otherwise it will be difficult to ascertain if the problem has been indeed solved by all the compounds claimed considered as obvious modifications or equivalents to one or more particular examples.

Industrial applicability
For the assessment of the present claims 28 to 31 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2004/032928	22 April 2004	9 October 2003	10 October 2002